U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

PUBLIC HEALTH SERVICE

FOOD AND DRUG ADMINISTRATION

TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHIES
ADVISORY COMMITTEE

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MEETING

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THURSDAY, APRIL 16, 1998

The Committee met in Versailles Rooms I and II, Holiday Inn, 8120 Wisconsin Avenue, Bethesda, Maryland 10814, at 8:00 a.m., Paul W. Brown, M.D., Chairman, presiding.

PRESENT:

PAUL W. BROWN, M.D.	Chairman
WILLIAM FREAS, PhD	Executive Secretary
DONALD S. BURKE, M.D.	Member
LINDA A. DETWILER, DVM	Member
LEON FAITEK	Member
BARBARA W. HARRELL, MPA	Member
DAVID G. HOEL, PhD	Member
WILLIAM D. HUESTON, DVM, PhD	Member
LAWRENCE B. SCHONBERGER, M.D.	Member
PETER G. LURIE, M.D.	Temporary Voting Member
DORIS OLANDER, DVM	Temporary Voting Member
ELIZABETH WILLIAMS, PhD	Temporary Voting Member
DON FRANCO, DVM	Industry Liaison
DOUG ANDERSON	Speaker
DAVID ASHER, M.D.	Speaker
RAYMOND BRADLEY, FRCVS, FRCPath	Speaker
BOB BREWER, DVM	Speaker
YUAN-YUAN CHIU, PhD	Speaker
KIKI HELLMAN, M.D.	Speaker
THIERRY SALMONA	Speaker
REINHARD SCHRIEBER	Speaker
WILLIAM STRINGER	Speaker
DAVID TAYLOR, PhD	Speaker
CAROL VINCENT	Speaker

ALSO PRESENT:

SUSAN ALPERT, M.D., PhD
CHARLES GREEN, PhD
JOHN HONSTEAD, DVM
MITCH KILANOWSKI
LARK LAMBERT
PHILIP MERRELL
ROBERT G. ROHWER, PhD
DENNIS WALKER

PUBLIC COMMENT:

LAURIE CLARK
JEAN LOW

I N D E X

INDEX: (continued)

P R O C E E D I N G S

Time: 8:03 a.m.

DR. FREAS: Good morning. Would you take your seats, please.

I would like to welcome you to this, our second day, of the Transmissible Spongiform Encephalopathies Advisory Committee. Now I would like to go around the table and introduce to you those members of the Advisory Committee who are at the table.

Starting on the audience's right is our industry liaison representative, Dr. Don Franco from the National Renderers Association.

Sitting next to Dr. Franco is Dr. Raymond Roos, Chairman, Department of Neurology, University of Chicago.

Coming around the corner is Dr. Linda Detwiler, Senior Staff Veterinarian, U.S. Department of Agriculture.

Our Chairman, Dr. Paul Brown, Medical Director, Laboratory of Central Nervous System Studies, National Institute of Neurological Disorders and Strokes.

Next to Dr. Brown is Dr. Donald Burke, Director and Professor, Center for Immunization

Research, Johns Hopkins University.

Around the corner is Ms. Barbara Harrell, our consumer representative, Director, Division of Minority Health. That's for the state of Alabama, Department of Public Health.

Next are our three temporary voting members for today. They are Dr. Peter Grant Lurie, visiting assistant research scientist, University of Michigan; Dr. Doris Olander, research associate, University of Wisconsin; and Dr. Elizabeth Williams, professor, Department of Veterinary Science, University of Wyoming.

The following members could not be with us here today. They are: Dr. Stan Prusiner, Dr. Edmund Tramont, Dr. Katherine O'Rourke, Dr. Dean Cliver, and Dr. David Hoel.

The conflict of interest statement that was read into the public record yesterday remains in effect today, and will remain in effect for the rest of the meeting and, therefore, will not be reread into the record.

Dr. Brown, I turn the meeting over to you.

CHAIRMAN BROWN: Thank you, Bill. It's too bad we have a few extra presentations. I see we've got some late sleepers. We could take a quick

vote. Oh, well.

We have a final presentation from the industry this morning, and then it will be followed by a couple of presentations by government, USDA and FDA. The industry presentation will be by Doug Anderson, titled "Continuing Perspective in Rendering." Mr. Anderson.

MR. ANDERSON: Thank you very much.

This morning I really only want to take the opportunity to summarize a little bit of what you were presented yesterday, to be sure that if there are any questions that those can be cleared up, and again talk about the rendering industry, which is essentially the environmental service provider of essential services to the food processing industry

It's something that we have been doing commercially for more than 160 years, and it's very notable that meat and bone meal has been used in animal feed for more than 75 years in the United States.

You were given descriptions yesterday about edible fat processing, about inedible fat processing, and I think the one thing that you do have to recognize and understand in the United States and that is that, if it's edible, it's edible because of

Federal inspection. That's what makes our food products edible versus inedible in the United States.

It's very possible, probable and practical that products that are made edible are then used edible, but they can also be used inedibly. Once a product in the United States is classified as inedible and unfit for human consumption, it is not allowed back into the human food chain. It can be deemed classified for inedible processing and recycling and reused in the proscribed manners already described.

The production: You've had a sufficient description. As in industry, because of the disease related issues, there have been many initiatives taken in order to protect the American consumer, our cattle feed, our human feed, and entirely across the board.

Traceability is one of the very important things that the use of HACCP programs, the use of ISO programs, any types of quality assurance will require -- do require and are being put into place and have been put into place by our industry. It's something that will further the protection of the food chain as we know it.

Edible products, again, can be produced under Federal inspection by a company that can have any owner. There are inedible captive renderers who

own edible rendering plants. There are meat packers who produce edible meat that have inedible rendering plants.

So it has to be very carefully looked at to make sure that we don't get caught up in a definition as we're looking at where the product comes from, where the product goes to, and whether or not it has been under Federal inspection.

I thank you for your time. I'm available for any questions relative that may have come up to you since the presentations yesterday. Thank you for your time.

CHAIRMAN BROWN: Thank you. Does the committee have any questions for Mr. Anderson? Ray?

DR. ROOS: So -- Yesterday I think we heard Dr. Taylor's results which suggested that a particular processing was optimal from the point of view of decreasing infectivity most significantly, and on the basis of that recommendations were made in UK and, in fact, the whole European Union.

I wondered what the impact would be on the renderers in the United States if such a recommendation was made or a guideline made, and how you yourself would feel about that.

MR. ANDERSON: The industry typically will

follow any guidelines, recommendations and rules that are made by the government. However, we feel that any of those rules and regulations should certainly be scientifically based, and they should certainly relate to diseases that exist within the area and the region that those recommendations are made for.

CHAIRMAN BROWN: The second part of that question, though, was what impact would that have on the rendering industry in terms of changing to that method. Is it going to require the stripping down of every rendering plant in the United States and rebuilding it? Is it a minor modification? Tell us about that.

MR. ANDERSON: It would virtually require the rebuilding of every rendering plant in the United States in order to -- I presume you're referring to the 3bar recommendation.

CHAIRMAN BROWN: Yes. Was that also true in Europe? Did it require rebuilding all of the rendering plants in the UK? And if not, why not?

DR. TAYLOR: I think, generally it's, if not total rebuilding, it required quite a lot of add-on expense. I don't know the precise scale of it.

CHAIRMAN BROWN: Ray, do you have any comments?

DR. BRADLEY: No, but in the UK, of course, we're not feeding any meat and bone meal at all to any food animal species. So the requirement is not in place. We're not actually processing all our material at 133 3bar 20 minutes.

CHAIRMAN BROWN: What are you processing?

DR. BRADLEY: According to the first Commission decision, which eliminated the first two processes which David showed us yesterday in regards to BSE ineffectiveness in decontaminating BSE infectivity. So we're operating satisfactorily in that regard, but not to take out scrapie agent as well.

CHAIRMAN BROWN: All right. Let me recapitulate. What exactly are you rendering or requiring to be rendered, according to David's minimum standard?

DR. BRADLEY: Nothing.

CHAIRMAN BROWN: Nothing?

DR. BRADLEY: Nothing.

CHAIRMAN BROWN: Who is? What's its purpose then?

DR. BRADLEY: Yes. The rest of Europe has to do that.

DR. DETWILER: I asked this yesterday, but

how many really -- We've tried to find out how many countries really have retooled all their plants, and we have yet to have been able to find that out.

DR. BRADLEY: In some countries, of course, long before the Commission decisions were made, either of them, they were already using 133 3bar 20 mins or very, very close to that, which made it a fairly simple process to adapt to the new rule; but -- Pardon?

DR. HUESTON: That's the Germans.

DR. BRADLEY: Yes, and some other countries.

DR. HUESTON: Some of them anyway.

DR. BRADLEY: I think Austria and --

DR. HUESTON: Not all of them.

DR. BRADLEY: Not all of them, no, and there are certainly plants in France, for example, which were not operating to that, and they would have to come to that standard, according to the Commission decision. Whether or not they have done so is a matter for their governments to tell you.

My understanding was, as I mentioned yesterday, that those plants which were operating below the required standard were only being used to render poultry material which, of course, is not

subject to that temperature restriction.

CHAIRMAN BROWN: So the sense of what the European Union is doing is that they are not recommending this minimum rendering temperature and pressure in any country or for any material that is judged to be either minimal or zero risk.

DR. BRADLEY: It's for all mammalian waste.

CHAIRMAN BROWN: I'm sorry?

DR. BRADLEY: All mammalian waste has to be rendered under the Commission decision to this standard, 133 3bar 20 mins. That is the Commission standard for all member states.

CHAIRMAN BROWN: Including the UK?

DR. BRADLEY: If it is to be used as feed for cattle, any species -- any species.

CHAIRMAN BROWN: Or process or go into tallow or gelatin.

DR. BRADLEY: Well, it wouldn't apply to gelatin, because that's a completely different manufacturing process. For tallow, that's not a requirement for tallow. It's only in regard to meat and bone meal.

CHAIRMAN BROWN: Okay. So the recommendation is only in regard to meat and bone

meal.

DR. BRADLEY: No. The Commission decision is very clear. It is ruminant -- Sorry -- mammalian waste that all has to be processed by this procedure before it can be utilized in animal feed as meat and bone meal.

DR. ROOS: So isn't that tallow?

CHAIRMAN BROWN: Waste would include tallow.

MR. ANDERSON: No. The way that it's being done is only for mammalian meat and bone meal, because the Commission decision allows pressurization of the meat and bone meal after it's been rendered. As long as the meat and bone meal has been subjected to the 133 3bar for 20 minutes.

CHAIRMAN BROWN: So the renderers in Europe would render any way they have been rendering, but the meat and bone meal part or greaves of that rendered material would have to be further rendered or subjected to the standards of temperature and pressure?

DR. BRADLEY: Exactly, if it was to be fed back to animals.

CHAIRMAN BROWN: Yes, but if it was to go into a tank, then you wouldn't --

DR. BRADLEY: Yes.

DR. ROOS: But some of the tallow is used in feed.

MR. ANDERSON: And tallow is not subject to the requirement, even in Europe. Tallow is --

DR. ROOS: Didn't you say that anything used in feed --

DR. BRADLEY: I'm sorry?

DR. ROOS: I thought you said anything used in animal feed. So if animal -- If tallow is used in animal feed, wouldn't it be subject to this? No?

MR. ANDERSON: Meat and bone meal.

DR. BRADLEY: It is related to the feeding of meat and bone meal to animals, and in the UK with this idea not to feed this to any food animal species, not even to pigs or to poultry. In the rest of the Community, all countries feed meat and bone meal to pigs and poultry, but such meat and bone meal must be processed by this procedure.

CHAIRMAN BROWN: Okay. So it seems now reasonably clear. You render according to your inner lights, and if the meat and bone meal product from that rendering is going to have any use, then it gets subsequently re-rendered or subjected to the standards

of temperature and pressure that David mentioned to us. If it is not going to be used for animal feed, then it need not be further processed. Is that correct?

Are there any other questions? Yes? Comment from the floor.

DR. MERRELL: It was my understanding yesterday that the tallow had no BSE infectivity in this process at all and, therefore, it's not included.

DR. BRADLEY: We can't hear.

CHAIRMAN BROWN: He said that it was his understanding yesterday that, since tallow is noninfectious, it doesn't need special consideration. Of course, that's exactly what the committee is going to decide.

DR. TAYLOR: Yes, on face value that could be a reasonable interpretation of the data, but in the presentation I'm about to give, I'll explain what the pitfalls in that argument are.

CHAIRMAN BROWN: Exactly. If everybody in the world had already decided that there was zero infectivity in tallow, we wouldn't be considering tallow. Right.

DR. ROOS: So we're going to break down the discussion into tallow and tallow derivatives?

MR. ANDERSON: Correct.

DR. ROOS: Maybe you could just clarify for me how much of tallow is used as a nonderivative form with respect to humans, and for what? I got the feeling some of it goes back to feed perhaps, but perhaps you could clarify that.

MR. ANDERSON: If it comes from the edible fat processing, it can be used in the human as a human food. It's used as a frying shortening. It's used in many foods, baking, etcetera, on the edible fat side. Okay? If it's edible tallow produced under Federal inspection, then that finds its way into a lot of human food.

Edible tallow produced as that specification can also find its way into inedible uses such as derivatives, oleochemicals, animal feed and such. On the inedible side, you have the fact that it goes for animal feeds. It goes for industrial products, cosmetics, etcetera, after further processing. It certainly doesn't go on just as tallow, but that also goes through other processing

CHAIRMAN BROWN: But the great bulk of edible tallow finds its way to human beings. That is virtually all of it. Is that right? Edible tallow.

MR. ANDERSON: I wouldn't say virtually

all, but I would say a large portion of it does find its way to human use, yes, of the edible tallows.

CHAIRMAN BROWN: Yes. Presumably because it's of a higher standard and, I suppose, is worth more per pound than inedible tallow.

MR. ANDERSON: Well, it's strictly based on the quality of the fat, based upon its color and its properties.

CHAIRMAN BROWN: Yes. So it would be sort of a waste to use it as animal feed.

MR. ANDERSON: Correct. It would be a very expensive choice as animal feed, yes.

CHAIRMAN BROWN: Larry?

DR. SCHONBERGER: To follow up a little bit on Raymond's question in terms of exposure of humans to tallow and tallow derivatives, I wondered if my concept that the human -- average human would be exposed to perhaps 10^2 more of a dose of tallow than of tallow derivatives on average. Is that a fair sense?

MR. ANDERSON: More tallow than tallow derivatives?

DR. SCHONBERGER: That if you were --

MR. ANDERSON: No.

DR. SCHONBERGER: That's what I'm trying

to get.

MR. ANDERSON: I would consider it the other way. There would be more opportunity for contact with derivatives than with the tallow, because it's the derivatives that go into the other products that are consumer used products.

DR. SCHONBERGER: By volume?

MR. ANDERSON: Probably by volume as well, yes. The oleochemical industry is a very, very large industry that consumes a lot of inedible tallow.

CHAIRMAN BROWN: I think we'll move on now. Thank you and, if there are further questions, there will be another opportunity in about an hour to ask them.

The next presentation, therefore, is going to be given by David Taylor, who has previously been introduced.

Incidentally, the next three presentations are all focused on the current regulatory policies with respect to tallow and tallow derivatives.

DR. TAYLOR: Thanks very much, Paul.

I've been asked to tell you about and comment on the kind of EU situation with regard to tallow, in which some opinions have been recently offered.

I suspect that there are probably representatives of industry here who have gone over these proposals with a finer tooth comb than I have. So I make any obvious errors, please do advise me here.

The question as to whether tallow is safe has been considered on a number of occasions in the past, and between the years 1994 to 1997, both the WHO, German Federal Health Authority and other respectable bodies have generally said, yes, it is safe. However, last year the EC multidisciplinary scientific committee cast some doubt on this. They basically were saying maybe not, let's look again, and they established a working group to look at the question.

We discussed yesterday some of the evidence which suggests that tallow, if not absolutely 100 percent safe, is certainly very low down on the risk scale. Initially, there was evidence from John Wilesmith's epidemiological study from which he concluded that the geographical variation in the incidence of BSE in the UK was not consistent with the distribution and use of tallow in cattle feed.

We discussed briefly yesterday also data coming from the spiked rendering studies involving BSE

and scrapie where, although we looked at only a limited number of tallow samples, a pair of tallow samples came from the processes which produced the least amount of inactivation as far as meat and bone meal was concerned.

So in the BSE run, we had meat and bone, in this case, affecting 50 percent of the mice that received it, but in none of the animals that received tallow from the same process.

Similarly, in the scrapie run the same process produced meat and bone meal which was infectious for 100 percent of the mice that were injected with it, but in none of the animals that received the tallow.

From these facts you can clear out with the figures of it. In the scrapie spiked run, 12 mice received a total of 6.245 mils of ten percent unfiltered tallow. So from that you say that, as that amount of material had contained 1 ID_{50}, then six mice on average would have been affected, but no mice were affected. Therefore, that volume contained less than 1/6 of an intracerebral ID_{50}, which is equivalent to 0.03 ID_{50} per mil. So that was in ten percent tallow.

Therefore, the neat tallow must have had less than .3 ID_{50} per mil. However, that was an

intracerebral dose. If you want to relate that to oral dose, Richard Kimberlin in the UK has produced a figure of 200,000 representing the difference in efficiency between intracerebral and oral dosing for BSE agent. This is scrapie, and he would admit, it's a fairly ballpark, crude type figure, but it gives you some idea of the scale of the difference.

That would be, therefore, equivalent to $10^{-4.2}$ oral ID_{50} per mil. If you accept the fact that there are no evidence to suggest that these diseases are ever or may be caused by cumulative dosing as opposed to single effective dose, then -- and you assume that the species barrier effect between cattle and mice is the same as for humans and mice, then you can say a human would have to consume almost 16 kilos of infective tallow over a short period to have a 50 percent chance of developing disease, even if there were minuscule levels of infectivity there.

I'm not saying this is a very precise set of data, but they do give you some idea, I think, of the relative risks.

CHAIRMAN BROWN: David, let me interrupt you for just a second. The other way to interpret, if you go back to the first slide, which is a slightly different read on the same data, is that it's true,

one mouse would have to consume 16 kilograms; but let's assume that one infectious unit were, in fact, present at the start, as you've said.

That means at some point, if those 16 kilograms are spread out amongst a million mice, that one of them is going to have a bullseye and die.

DR. TAYLOR: Oh, yes.

CHAIRMAN BROWN: In other words, if there's an infectious unit in tallow and there's nor eduction in that infectivity through processing, that infectious unit is going to find its way to somebody.

DR. TAYLOR: Oh, yes, sure.

CHAIRMAN BROWN: Okay. That's just -- I mean, there's a way to look at this that suggests, forget it, but there's always a way to look at it to suggest let's not forget it, and let's keep talking about it.

DR. TAYLOR: That's why I made the point that I'm not claiming these are very precise calculations, but giving you some ballpark idea.

Before going on to discuss the scientific steering committee opinion in Brussels, it's important to reemphasize things that were said yesterday, and that is that in the recommendations, they refer to risk factors for tallow which relate to the countries

of origin and the nature of the raw materials.

The problem is that the -- in Brussels, while there's not much difficulty in defining a high risk country and a country perhaps of unknown TSE status, they have not yet come out and said what their definition of categories 2 and 3 will be.

The other problem is, as you know, that what will eventually be defined as specified risk material has not yet been defined and will not be for sometime. The only inkling that we have at the moment of the way things are changing is that bovine lung is not likely to be an SRM.

There was a scare that infectivity would get into bovine lung as a consequence of the method of slaughter. It's now believed that this only applies to these very high pressure guns working on compressed air.

It's also considered that bovine ileum which, as Ray showed yesterday in the pathogenesis study, appears to become infected, can be sufficiently and reliably separated from the rest of the gut to be able to declare ileum only as a specified risk material, and the rest of the gut to not be.

Again, a bit of sitting on the fence as far as deciding about sheep tissues are concerned,

because what I read into what has come out is that they are waiting for some sort of risk assessment relating to the real risk of BSE being in sheep, at least in the UK.

They've categorized tallow into these four types: For human or animal consumption or application; for injection; for industrial use, but that's not for tallow derivatives; and category 4 for manufacturing tallow derivatives.

Now the question was asked before I spoke about guaranties and purity of tallow. Despite the data which I've shown which says we have found nothing in tallow, one has to accept that there is some degree of contamination of tallow with protein. Therefore, there must, at least theoretically, be the possibility of infectivity being in there at some sort of level, albeit very low, from time to time.

So one of the plights of the proposals of the SSC is to use purification processes with tallow which will remove protein, and these have been described to some extent yesterday involving either centrigation, filtration through diatomaceous earth, coagulation and then centrigation using phosphoric acid, combinations of the above methods.

The levels to which these should be --

these proteins should be reduced have been declared to be these levels, and that being equivalent to residual nitrogen levels of less than 0.02 percent, and that residual peptides or polypeptides should have a molecular weight of less than 10,000 daltons.

Either publicly or privately, I'd be interested to hear what UK renderers think of the practicalities of these.

Okay. As to the actual recommendations, where the material is for animal or human consumption or application and the raw materials are declared fit for human consumption -- this is by both antemortem and post mortem inspection of the abattoir -- then if the materials are from a high risk area, they're saying that you need to exclude the SRA, process the material by the 133 degrees Centigrade process, if the raw material is not exclusively from discrete and clean lumps of fat tissue, and you also apply a purification process.

This has caused -- this is the opinion. It has caused a bit of debate, because personally I think it's crazy, but you could go into your butcher shop and buy muscle, liver, kidney from animals in this category, and eat them raw in your own home, if you wished; but if you're going to consume tallow from

this animal which has come from anything other than discrete adipose tissue, you will have to autoclave it by this process. That doesn't, to me, hang together.

Category 2: If the raw materials are from lower risk areas, exclude the SRMs and apply a purification process.

CHAIRMAN BROWN: Excuse me, David. On that first point, how would you -- In the UK -- and let us suppose you've got a herd, is it -- are livers and kidneys and so forth and pancreas and thymuses which all would be specified as specified risk materials -- are they in the marketplace?

DR. TAYLOR: No, they're not specified risk materials under anybody's category.

CHAIRMAN BROWN: Spleen is not? Spleen, you don't eat anyway, but sinus.

DR. TAYLOR: Well, spleen is an SBO, yes So is thymus, but --

CHAIRMAN BROWN: I'm sorry?

DR. TAYLOR: Thymus and spleen are SBOs or SRMs.

CHAIRMAN BROWN: Right.

DR. TAYLOR: What I mentioned were tissues that you could go into your butcher shop and buy.

CHAIRMAN BROWN: Liver, for example.

DR. TAYLOR: Liver, pancreas, all legally.

CHAIRMAN BROWN: You could go in and buy a liver in any butcher shop in the United Kingdom now, and you wouldn't know -- well, maybe you would. Would that liver possibly come from a cow in a herd that had had a case of BSE?

DR. TAYLOR: Yeah, technically. Yes. It would be under 30 months.

CHAIRMAN BROWN: It would be under 30 months old?

DR. TAYLOR: Yes. All human consumption material must -- bovine material must be under 30 months at slaughter.

CHAIRMAN BROWN: But, of course, we know that viscera are infected early, if they're infected at all. What's the point of it?

DR. BRADLEY: Only the distal ileum in cattle, as I've showed in the pathogenesis study, not any of these other --

CHAIRMAN BROWN: Yes, so far. Right.

DR. BRADLEY: Well, no, complete, up to 30 months --

CHAIRMAN BROWN: No, no, no. I understand what you're saying. I'm saying, so far you haven't got any infectivity in any other organ, but we know in

the other TSEs that infectivity does occur in viscera, and it occurs early rather than late.

So what I'm saying is in principle, in a heard that had had BSE diagnosed, a cow or a steer from that herd that was clinically healthy would be butchered, and the liver could be --

DR. TAYLOR: Yes.

CHAIRMAN BROWN: Okay.

DR. TAYLOR: But as Ray said, the pathogenesis study is not showing anything in all these peripheral tissues. Okay.

If the raw materials are from a lower risk area, exclude SRMs and apply a purification process. if they're from a BSE free or negligible risk area, apply a purification process.

What to say about countries with an unknown TSE status is try to carry out a risk assessment and, if you can't do that meaningfully, regard it as high risk. This suggests to me that, because the country is described as having an unknown TSE status make sit unlikely to be able to carry out a meaningful risk assessment, and you'll be forced into describing it as high risk.

The second category is tallow from -- for animal or human consumption application where the raw

materials are unfit for human consumption. Again, the SSC are sitting on the fence, because they are in a bit of a dilemma, because they know that within that category, at least within the EU, the raw materials can and will include fallen stock, condemned carcasses, sick animals, zoo animals and even laboratory animals.

So they have still to define the minimum processing conditions, and the interim recommendation is that anything that comes within that category at the moment should be fed only to animals, even in BSE-free countries, because of the risk of sporadic case of BSE.

One of the categories was tallow for injection. This is not to be confused with tallow derivatives -- tallow for injection, and there are, at least within the EU, currently no known examples of this.

For industrial use but not for tallow derivatives, if the materials to be used are fit for human consumption, the only restriction is that you apply a purification process. That policy changes as the raw materials are unfit for human consumption.

I think the ethos here is that people using large volumes of tallow based product in the

industrial setting may be unaware of what they're handling, and so you do have to protect them in some fashion. So the recommendation is a process by the 133 pressure system, and apply a purification process.

Further, they say that if the end use is unknown -- in other words, you can't guaranty that people are sloshing around in this stuff -- that the conditions relating to the different geographical sources as applied to human consumption material derived from raw materials fit for human consumption should apply.

For the production of tallow derivatives, if the materials are fit for human consumption, there appear to be no restrictions; but if you're using any other type of raw material -- it's relatively vague, but the way I read it is that you use procedures that are inactivating for BSE agents during the manufacture of the tallow derivatives.

I think Dr. Green yesterday gave us a rather convincing and eloquent demonstration of the fact that the procedures that are used for, as far as I could gather, all of the tallow derivatives are -- would be considered to be fairly reliably inactivating for TSE agents.

Now we're not talking about procedures

that have actually been validated, but -- with regard to that characteristic, but over the years these procedures have been looked at by a number of committees who have all concluded that they cannot conceive of TSE agents surviving these splitting type procedures.

So I think we could probably regard these as -- generally regard it as safe type procedures.

That's my understanding of the SSE opinion, but if anybody has spotted any major blunders, I'd be happy to hear from them. Thank you.

CHAIRMAN BROWN: Thank you, David.

The European solution reminds me a little bit of Schedule D of the IRS form. Lord, I hope that we don't get into that. That's a very complicated set of recommendations.

Are there any questions for David? Linda

DR. DETWILER: Dr. Taylor, what prompted the SSC -- or the MDSE, I'm sorry, to say maybe not Was there something specific or was it just a limited data, because it's a difference -- right? -- from earlier rulings?

DR. TAYLOR: You mean what prompted them to look at tallow again?

DR. DETWILER: Right. To say maybe not.

DR. TAYLOR: Well, as you know, the whole way in which the EC operates in terms of concerns about BSE and TSE has had a shake-up over the last 18 months, two years. It's my view that the previous system was actually very good, but that's not the way the EC actually considered it.

So new brooms sweep clean. I think with the concern, to be fair, over human health, the people in whose lots the responsibility now lay felt we have to relook at all of the existing data.

I don't -- I think maybe I went too far when I said that the MDSC said tallow is maybe not safe, but to be more realistic, I think they said, well, perhaps we should look at this through fresh sets of eyes and convene a working group.

Is that your understanding, Ray?

DR. BRADLEY: Yes.

CHAIRMAN BROWN: Has anyone spiked tallow with a conventional virus to show that you can actually demonstrate infectivity in something with a consistency of tallow, one.

Two, how did you get the tallow into suspension for inoculation? I would have thought -- I know you made a one to ten. How did that work?

DR. TAYLOR: It actually emulsified not

too badly in a grinding tube. It just suddenly formed what to be a colloidal suspension.

CHAIRMAN BROWN: I don't know if --

DR. TAYLOR: The reason we used ten percent is that we couldn't get the big tallow through the needle into the --

CHAIRMAN BROWN: Yes, of course. You can't inject a candle into a mouse's brain, but it's a curious point about -- You know, I don't know if anybody -- I'm unaware of anybody trying to detect infectivity in butter, for example. I just don't know how you do it.

If there are no precedents for this material being able to have infectivity detected, I don't know what to think.

Other questions? Yes?

MR. ANDERSON: Dr. Taylor, in the one description of the peptides or the polypeptides, there was a pick of a molecular weight of less than 10,000 daltons. Is there some scientific basis for that, or what was that pick?

DR. TAYLOR: I guess it was probably a mix, a compromise of what was perceived to be achievable and based on the fact that the infectious core of the PrP protein is somewhere around 27,000

daltons.

CHAIRMAN BROWN: As far as I know -- and, Bob, you may be able to correct me -- there is no experiment on the books in which infectivity has been detected in any filtrate going through a 10kd filter. Is that correct?

DR. ROHWER: No. There are several publications which have claimed to find infectivity on the other side of alterfilters and nanofilters. However, none of those experiments have been controlled very well, and there's certainly a whole 'nother body of -- well, there's not a lot of data, but there are several other experiments which indicate that infectivity is not past a 30 nanometer track etched type filter, which has a very precise pour size definition.

CHAIRMAN BROWN: So there are sizing experiments on which that number is based. I guess there's no exact equivalence between sizing nanometers and kilodaltons. So you choose one or the other. Probably the securest data is based, as Bob said, on nanometer sizing rather than molecular weight sizing, but in general the size has been -- It's pretty small infectious particle, and that is the kind of cutoff that has been historically used as a good filtration

system for removing infectivity.

DR. TAYLOR: Can I just comment, Paul. I mean, I don't think this implies that you will or you will need to use molecular cutoff filters. They're saying that you can achieve that, even by filtering through reasonably deep beds of diatomaceous earth. That's my understanding of the situation.

CHAIRMAN BROWN: Thank you, David. I think we'll move on now to the final two presentations before the committee is required to make some decisions.

They will be, first -- Excuse me, three presentations. They will -- No, two. They will be, first, by Dr. Bob Brewer of the USDA and FDA,m and Dr. Chiu is also listed in both presentations. I'm not quite -- Okay. Doctors Brewer and Chiu, in some order.

DR. BREWER: Well, I'll just try to amplify a bit on what we said yesterday and, hopefully, answer a few of your questions. FSIS is also a low tech/low budget operation. So we'll resort to overheads, too.

Our conversation today is basically around tallow, of course, and it was kind of interesting to look at tallow. Would you put the next overhead on

there, please?

I looked at Dorland. That seemed to be a good place to start with this crowd, and it was a very concise definition. Tallow is described as suet. The next definition, please.

Yo look at suet in Dorland, and it says it's the fat from the abdominal cavity of a ruminant in the preparation of cerates, ointments and as an emollient in pharmacy use. It is the external fat of the abdomen of a sheep. That probably is a reflection of what Dorland is involved with, and I don't think we can produce any -- as far as I can determine, we are not producing any edible tallow from sheep in the United States.

Next slide, please. This is Webster's International Unabridged dictionary. It's rather old, but it's, I thought, a pretty good definition: Animal fat, suet, rendered fat of cattle, sheep, composed of glycerides, etcetera, used to manufacture soap, glycerol, margarines, and lubricants.

The last, please. This is an interesting dictionary that USDA provides to us. It's not a very reliable dictionary. You should look further most of the time, but they're talking about tallow as being a product from the bodies of cattle, sheep or horses,

and again certainly there's no edible tallow from horses being produced in the United States.

Okay. There's a little interesting commercial fact about tallow. It's long been a factor in the United States or in the land of the United States. The California Spanish missions were set up by Spain for three purposes. One was to control the land for Spain, of course. One was to save souls, and one was to be a commercially viable operation. I'm not sure in what order that was to be done.

Their are two main exports back to Spain were tallow and cattle hide. So we've had a long history of producing tallow in this country.

Next slide, please. FSIS's involvement with tallow comes under Title 9 of the Code of Federal Regulations, and these are the various parts, and it's very scanty. There are four different parts listed there, but probably it would take you about three minutes to read all four parts of it. Take you longer to find them than it would be to read them.

Next slide, please. I think this is a crucial point for this crowd. All raw material for edible tallow has to come from an officially USDA inspected plant. It has to be from inspected and passed animals. It has to be from a recent production

lot.

In other words, you can't accumulate this tallow, have it around in storage for a couple of months and then decide to produce an edible tallow from it. It has to be kept in good condition, stored at 50 degrees or less before it's processed, and unless it's moved directly from the kill floor or the rendering units.

Now from a practical standpoint, most of the tallow in the United States comes from a very few plants. I think Dr. Franco mentioned yesterday that we don't have a lot of plants producing edible tallow. We have -- USDA inspects approximately 1100 slaughter plants. Fifty of those 100 plants produce 85 percent of the production.

We've got -- These plants -- Some of these cattle plants are killing as much as 7200 head a day. A number of the swine plants are killing 15,000 swine a day, and they produce -- One plant kills 22,000 swine a day, and we only have five sheep plants that kill 90 percent of the lambs in the United States.

So we don't have a lot of the plants that actually wind up producing this edible tallow. Certainly, no more than 50 plants are producing edible tallow products, and these are all USDA inspected

plants.

Any of these plants that bone away from a USDA inspected plant or fabrication plant are not, for the most part, as far as I can determine, producing any edible tallow. That all goes to the inedible tallow.

In the USDA inspected plants, these animals are, as I said yesterday and I'll repeat -- they are inspected at movement, and they're inspected at rest in the corrals. If they pass that inspection, they go into the plant. They're slaughtered. They're inspected again by another inspector, and in the big plants these are lay inspectors. That is a fact of life.

Then if they pass that inspection, they proceed on down the line. They go through the final stages of processing before they go into the coolers, many of these plants are now using steam or hot water pasteurization. They're rinsed in a steam cabinet or they're exposed to live steam in a steam cabinet, or to 160+ degree water and a 20-second rinse, and then many of them go from that rinse into an acidic acid rinse, two percent acidic acid, and rinsed again, and then they get a final just potable water rise and go into the chillers.

Then there in the chillers, they're held there for 24 hours up to 36 hours where they're chilled; and while they're in these chillers, they are spray misted for 60 seconds every hour with a 20 parts per million water spray. That helps reduce the temperature down.

So up until a couple of years ago, most plants were holding these animals 24 hours before they started breaking them down and fabricating them. Also at that time, some of them were removing the fat at the end of the line, the so called hot fat removal.

Well, that did not produce the results they thought it would. The idea of that originally was to reduce the energy requirement for cooling the carcasses, and it didn't make any difference.

So they've gone back to chilling them now, and then they remove that fat 24-36 hours after they're killed and before they're fabricated, and that is the fat and the fat that's derived from the fabricating processes that winds up in most of the edible product in the United States, and that's virtually all that winds up in the edible tallow.

Once it goes from off that kill floor and goes into the rendering process, it is put into rail cars or trucks and moved to some other establishment,

and at that time when it's put into the cars or the trucks, it's sealed by USDA, and that's the end of USDA's involvement in it.

So where it goes to -- and after that, it falls under other jurisdictions.

I would like to mention one thing that kind of bothers me a little bit. I've practiced for 32 years and I have a lot of family involved in the livestock business, and we keep hearing the fact that there might be one animal per million with BSE each year in the United States, and we're not finding that.

Well, we have about 110 million cattle. So that would translate to 100 head of cattle or so, and I strongly believe, and I think most veterinarians in this room would agree with me, that if there's 100 animals out there with BSE in the United States, somebody sure as hell is going to find them, because he would have his career made. It would be a real feather in his cap.

I think, at the same time, any people that are routinely losing animals that are producers, like my brother died three years ago. At the time he was milking about 2,000 cows; and if he was losing a cow or two a year, he would know about that, if it was BSE. He would certainly take it to somebody and find

out what was happening.

So I really don't think that it's a viable option to talk about missing all these BSE animals out there.

Then finally, I want to make a few comments about the downer cow or the non-ambulatory cow issue. That is a bit of a can of worms, to be frank about it. There are a lot of different sides to it. There's a humane issue, certainly; but again, an awful lot of the so called downer cows or non-ambulatory cattle are animals that are injured by one way or another.

I was in a plant two weeks ago in California that ordinarily gets about 20 of these cows a day. Most of the time, they're Holsteins that have slipped on cement and, if a Holstein tries to get up two or three times, is not successful, they no longer try.

So different lengths of time they're allowed to remain on the farm, because these people's hope springs eternal, but most of them do wind up at a slaughter facility to be slaughtered or attempt to be slaughtered, salvaged for something. But at that time, because of the rains and the conditions that had been existing in California and is attributed to El

Nino, they were getting 90 downers a day in there.

A lot of these cows are being injured in the process of the conditions that existed in the corral. So an awful lot of the downer cattle in this country are due to injuries. So I think that that's something that, again, I personally don't perceive the downer cow as being a great source of problems to this.

I've kind of rushed through this, but I do want to reiterate that any edible tallow, I think, is adequately inspected at this point, and I think that the veterinarians are not primarily involved in inspecting for edible tallow production, but in part of their oversight in the boning rooms and in the slaughter floors, they are very careful to ensure that contaminated product does not get into the edible product line.

The final comment will be made about spinal cords. Again, from a practical standpoint spinal cords are not going into these advanced meat recovery systems for a couple of reasons.

Most of these spinal cords are removed either at the end of slaughter line or certainly very early in the hot boxes, because the spinal cords had a tendency to fall out on the floor; and when the

people washing the floors the next morning in the coolers wash these down the drain, then you have to call Rotor Rooter to dig them out.

So they're very careful to take them out, and they were selling them for a while; but that market is pretty well collapsed, too. I was talking to a packer the other day, and he said they're so cheap that it does not pay them to salvage those. They were sending quite a lot of them to Japan and to Central America.

So if I can answer any questions, I'll be around here all day. I'll certainly try to do that. Thank you.

CHAIRMAN BROWN: Questions for Dr. Brewer? Yes?

DR. OLANDER: How does the inspector evaluate the neurologic status of a non-ambulatory animal?

DR. BREWER: Well, those animals are inspected by veterinarians, and it's somewhat subjective. I'm not going to pull your leg, but I think most of these people have been there a long time, and it's -- they can't do a CAT scan or anything that esoteric, but I think that most of them -- I don't think that's a particularly difficult thing to

do, to determine the central nervous status of an animal.

Now if you want to back up a little bit and we'll get Linda involved in this, I think that some of these downer cows come in, and they should not be brought to slaughter plants. I think they should be examined before they leave the farm or the ranch or the dairy and be examined by an accredited veterinarian. A lot of those animals wouldn't arrive there, because they come in comatose. Well, then they're condemned anyway.

DR. OLANDER: What is the role of state inspection -- state inspected plants in the tallow flow?

DR. BREWER: In tallow flow? Well, for the most part, state plants are very small entities. Even USDA -- We have plants that kill ten head a year, believe it or not, and we provide Federal inspection to them. It's just not a very good use of resources, but we do that.

Some of the small state plants are down in that kind of number, too, and there really aren't any large state plants, but state plants have an inspection system that's supposed to be the equivalent to, but as far as I can determine, none of the state

plants are producing product that goes into edible tallow. That all goes into inedible product, as far as I can determine.

CHAIRMAN BROWN: Thank you very much. Dr. Chiu.

DR. CHIU: Good morning. I would like to thank the committee for coming and spending time in helping us to make a very important decision. I would also like to thank all the people. You provide a very valuable information, and I also would like to thank all the FDA staff for helping us to prepare this meeting.

I'm going to give you a review of FDA policy and the requirement on tallow and the tallow derivatives. I'm going to go over the related use, the use of tallow and tallow derivatives regulated by FDA, and also the current product quality standards, FDA inspections, and also the susceptibility of countries for sourcing.

Next slide. The regulatory status of tallow and tallow derivatives in FDA relate is based on its end use. Yesterday we have heard edible tallow and the hydrogenated tallow can be used as food, also can be used as food ingredients or food additives.

We also know inedible tallows from a

renderer can be used in animal feeds. Both edible and the inedible tallow and the tallow derivatives are used as a component of many cosmetic preparations. FDA does regulate cosmetics for human use, but not for animal use.

We also learned, most likely, edible tallow derivatives are the ones used for human and animal drugs. Although we do not have official data in-house on dietary supplements, however, because dietary supplements are prepared either like food or like a drug, therefore, the use of tallow and tallow derivatives for drugs and foods probably applicable to dietary supplements.

Next. We also heard the limited tallow derivatives such as glycerin being used in medical devices and in biologics. How those uses are really used of these tallow/tallow derivatives as a component of the final product. However, tallow derivatives such as the surfactants or glycerins are also used in a different way; that is, to be used as a reagent in the manufacturing of bulk drugs or medical devices.

Next slide. Next I'll give you a little bit of marketing data we have in FDA. The data presented in this slide is a 1992 data for tallows consumed/sold in this country.

You see there are 693,000 metric tons of edible tallows sold as food or used in food. Out of this, 194,000 metric tons are sold for -- as frying fat in places such as McDonald's. So it translate into like seven grams per day per person.

Regarding edible tallows in 1992, 1,400,000 metric tons was sold. More than 50 percent of that is used in animal feed. We also have data showing 20,000 metric tons of edible tallows are imported. It constitutes less than three percent of the market by volume.

You have this slide in your handout -- next one. The next slide you have in your handout. It may not be very visible from the screen.

This slide gives examples of tallow derivatives or tallow used as food or in food or in cosmetics. In FDA there is a voluntary registration program for cosmetics. There are over 16,000 cosmetic products marketed in this country. However, much less of that number has been registered at FDA.

On the lefthand side are the substances used in the cosmetics, and on the righthand side is the number of products contain those substances. Because a product may contain multiple substances on this list, therefore, the sum of the number of

properties is less than the number of products.

Next slide. This slide is also in your handout. It is used to illustrate the wide use of tallow derivatives in pharmaceuticals. On the lefthand side, the left column, we put the causes of oleochemicals used in pharmaceuticals.

They are fatty acids, fatty acid salts, fatty alcohols, fatty acid esters, tallow glycerides; and the polyglycerides, triglycerides, diglycerides, and the monoglycerides.

After that will be fatty nitriles and the amines and the glycerins. The substances under each type of chemicals are just used as examples. The common ones are listed. There are many others not listed in this table.

The middle column gives you the information on the functions of those substances used. They serve either as emulsifier agents, solubilizing agent, lubricant, dispersant, and have warming agent, surfactant, antimicrobial preservatives, waxing agent, solvent perentals, sweetening agent.

All those components are substances that are in the final formulated dosage form. So they are a component of the drugs. Under the dosage forms and the route of administration of these products cover

almost every possible dosage form and every means of administration.

CHAIRMAN BROWN: Dr. Chiu, excuse me. Is toothpaste included somewhere?

DR. CHIU: Yes. Toothpaste is considered oral. I think it's an MPC.

CHAIRMAN BROWN: Well, that's okay.

DR. CHIU: I don't think --

CHAIRMAN BROWN: I just wondered if toothpaste were one of the -- considered a cosmetic in that sense.

DR. CHIU: No. Toothpaste can be considered either cosmetic or as drugs. If toothpaste has prevention of a disease such as tartar prevention, then it becomes a drug. So some of the toothpastes are regulated as drugs, but this list does not include toothpaste. So probably either our data is not complete or because they did not use one of those components.

CHAIRMAN BROWN: And are tallow derivatives used in toothpaste?

DR. CHIU: I have to go back to check, because my list does not include toothpaste. If toothpaste is used, we would consider it sort of like a oral drug.

Next one. So because the tallow and tallow derivatives are widely used in FDA regulated products, so they have different regulatory status. As you heard from Dr. Brewer, once the tallow leaves the rendering plant, then it's under the jurisdiction of FDA.

So under the food regulations, then tallow to be used in food, then it will be covered by the food good manufacturing practices, and also where it needs to meet the food labeling requirements.

There is no need to submit application for premarketing approval. The only substances which require FDA premarketing approval for tallow or tallow derivatives in area of food is for food additives.

Many of the tallow derivatives are considered generally recognized as safe. So those substances would not require premarketing approval. They would need -- Many of them meet food chemical Codex standards, and for tallows we heard yesterday, the standards -- quality standards and specifications are established by the American Fat and Oil Associations.

The components used in cosmetics actually are very loosely regulated by FDA. It does not require premarketing approval, and that is the color

additives.

Then for drugs, the tallow derivatives -- Tallow is not used in drugs, but tallow derivatives are. Because they do not serve a pharmacological function, they do not have pharmacological activities. So we consider them an inactive ingredient, and collectively we call them excipients.

Many of the tallow derivatives are GRAS substances, and they meet either Pharmacopoeial or National Formulary standards, and they also will need to meet other standards established -- is established in our Code of Federal Registry.

Next one. Because the tallow derivatives are either food or most likely for the ingredients -- most likely, they are GRAS and they are also excipients meeting USP or NF standards. So ordinary submitting documentation on its manufacturing process and the quality controls to the agency usually are not required.

FDA rarely inspects the manufacturing establishments of drug excipients. What we -- in the pharmaceutical area, what FA inspects are the pharmaceutical manufacture of the active bulk drug and the dosage forms. We make the pharmaceutical manufacturer responsible for the quality of the

excipients used, as approved by the agency in the application.

Next one. The next two slides will give you an example of what kind of quality standards we're talking about. The first example is fatty acids as food additives, which is listed in 21 CFR 172.860.

It stated -- The regulation stated fatty acids must be derived from edible source. It contains not more than two percent of unsaponifiable matter by using a method specified in Association of Official Analytical Chemists.

Then it also must be free of chick-edema factors. You can either use a bioassay or use a GEC methods specified in AOAC.

The next example is USP grade of glycerin. The Pharmacopoeia stated that glycerin must contain 95 percent to 101 percent of the glycerin molecules. Then you provide passive specification for chemical identity, physical property, and purity, in addition to assay.

So from these examples, you see none of the quality standards would address the safety related to the BSE.

Next one. So in order to assure that bovine derived product will be safe in the context of

BSE and not contaminated by BSE agent, the agency has taken a series of actions. The agency -- As you heard yesterday from Dr. Bailey, the agency has issued a series of letters and published notice in Federal Register, and also issued new guide -- new regulations on feed ban and also issued a guidance document on gelatin.

Next one. The essence of those recommendations issued which are applicable to tallow and the tallow derivatives is illustrated here. The first one is the bovine source material: Not to use materials that have come from cattle born, raised or slaughtered in BSE countries, according to USDA.

The reason for this recommendation is we felt, in order to have safe product, you must have clean materials, to start with. Therefore, sourcing from the BSE-free countries we are assured the final product quality.

The second recommendation is about records keeping. The agency recommends to identify bovine derived materials used in FDA regulated products, and document the country of origin of the live animal source; maintain traceable records; and maintain records at the site of manufacture; and make them be available for FDA inspections.

Then later on we did -- In 1994 we did provide exemption of the requirement for BSE-free sourcing to gelatin, milk and milk derived products, and last year we revoked partially the exemption applicable to gelatin. However, there is no exemption up to today for tallow and the tallow derivatives.

Yesterday we were asked to provide you with a table to delineate the status of different substances in relation to its use. So this table was made last night.

On the lefthand side, the left column, we have the substances, gelatin, edible tallow, inedible tallow and the tallow derivatives. The first row specifies all the different types of product. The first one is injectable, ophthalmic, implantable products, followed by oral products. That includes food, oral drugs, dietary supplement, nutrition supplement.

The third columns are drugs administered the other routes. The fourth column, cosmetics, then followed by animal feeds.

The "yes" and "no" in the database stand for the acceptability of BSE countries for sourcing. So if it's stated no, it means BSE countries are not permitted. If it says yes, it means it is permitted

with or without restriction.

Under gelatin other drug products, I put down yes. However, based on our database, a very few products other than oral products contain gelatin. So, therefore, our gelatin guidelines did not specifically mention products administrated by other means than oral or injectable.

Then in parenthesis, when I say not used, it means we have not identified that substance used in that product. I was advised this morning under animal feed, edible tallow was specified not used may not be complete true. It depends on the price. So when the price is good, the edible tallow may be used in animal feeds.

I'll stop here and answer any question you have, then go on to next one, the questions.

CHAIRMAN BROWN: Yes. Thank you, Dr. Chiu. Any questions for Dr. Chiu before we move on? Are you now going to read us the questions we are to address?

DR. CHIU: And I'm going to give a little background, then have questions -- then go on questions. Yes?

DR. SCHONBERGER: You said in your talk that the average person -- or the tallow consumption

in the United States came out to about seven grams a day per person. I had asked that -- I'm trying to get the sense of exposure to these various products to an average person in the U.S. and compare tallow with tallow derivatives. I'm more interested in the comparison.

I was under the impression before this that we were more exposed to tallow, because I can see that. I go to a hamburger joint or something and get french fries, and I'm getting exposed to tallow, and I can, you know, go to a bakery and I'm exposed to tallow, get some soup or something like that.

The derivatives seem to become -- I get exposed to in very small amounts like if I take a pill or something like that.

DR. CHIU: Exactly.

DR. SCHONBERGER: But I was just told that I'm more exposed to the derivatives than I am to the tallow. So --

DR. CHIU: I think you are more exposed to the different kinds of derivatives, but in terms of quantity, if we are thinking about going through pills or dietary supplements, then the amount is very little. If magnesium stearate, typically the use is just a few milligrams per tablet, and actually most of

the filler we use in pills is lactose.

DR. SCHONBERGER: In your own -- So you're giving me another -- In your own view, my exposure to tallow versus the tallow derivatives by volume, the way you're thinking of it, is ten times greater, double or 100 times greater? What -- In your own mind, what kind of difference are you thinking in terms of in my exposure to tallow versus tallow derivatives? Just trying to --

DR. CHIU: Well, that's very difficult to estimate. It depends, first of all, whether you take pills routinely, whether you use cosmetics routinely, and also you use shampoos and other cleaning agents, and also we use soap every day.

So I think when you talk about all those combined, you may be exposed significantly, but if you want me to give a figure of five or three times, it's very difficult.

CHAIRMAN BROWN: You and I have less need for shampoos than most.

DR. SCHONBERGER: That's right. Exactly. I also don't wear that much cosmetics, but unfortunately, I go and eat a lot of food. Too much.

DR. HUESTON: If I understand your calculation correctly -- I didn't do the math, but

seven grams is actually the -- That's the total use of edible tallow divided by the number of people in the United States.

DR. CHIU: Right.

DR. HUESTON: And the vast majority of that is actually not consumed. When you go into the -- at least the last time I went to a fast food place, they didn't give me a little container of the grease to drink after I had my -- So the majority of that grease simply gets recycled or in some way -- It isn't actually totally consumed.

DR. CHIU: No. It's not all consumed. It's sold, though, and it's sold to fry french fries. You eat french fries. You will not eat the grease. Most of the grease probably is just throughout. DR. HUESTON: So it's probably safer to say that it's seven grams of edible tallow that's sold as opposed to consumed.

DR. SCHONBERGER: Will, what's your assessment of the exposure? You know what I'm trying to -- Do you have your own sense that we're more exposed to derivatives?

DR. HUESTON: Well, I was interested by the -- That's why I asked this question, because I was fascinated. My gut feeling is the same as yours, that

our exposure to tallow is greater than our exposure to tallow derivatives in terms of a volume.

I'm interested -- Doug, throw it back at him.

MR. ANDERSON: If you're talking about how much do you eat -- I mean, if you talk about the tallow that you consume as being part of the steak or part of the hamburger that you eat, that's an entirely different story, because that's not tallow produced as tallow. That's a human food that's being, you know, worked out in the fast food restaurant.

When you talk about going to a fast food restaurant and eating fries, unless you don't remember what Mr. Sackalov said USA Today a few years ago, most every fast food restaurant in the United States doesn't use edible tallow to fry their french fries. They use vegetable oils.

So, you know, I think that when you talk about an exposure situation from eating french fries, you're probably not going to come into contact with any of the edible tallows anyway. If you talk about fat consumption as part of the foods that you eat, that's an entirely different topic than, I think, what we're talking about here today.

Here we're talking about tallow that's

been produced in an edible fashion from Federal inspected plants. And that's where I'm coming from.

CHAIRMAN BROWN: Excuse me just a second. Dr. Brewer, did you have a comment? We're starting to lose a little --

DR. BREWER: I wanted to make a comment that would go along with what Doug was saying. One of the companies told me last week that in 1990 they had ten plants producing edible tallow, and as a result of what's happened with the french fry market going to vegetable shortenings, they now have one plant producing edible tallow, and nine of those plants are producing tallow, what they call technical tallow, that goes into soaps, and it's enough -- all these bird feeders.

They're selling huge tons of that, these little square blocks of bird seed. So they probably make more money doing that, but also it's going into some dog foods, too, but they've gone from ten plants to one plant.

CHAIRMAN BROWN: Dr. Chiu, is this -- In what way will this presentation depart from the previous one? What are we now --

DR. CHIU: Oh, it will be a little different, just two slides, and then will be

questions.

Before we discuss the questions, I would like to mention the factors which has impact on the safety of tallow and tallow derivatives. The first factors we'd like you to consider is source materials, the sourcing country and its BSE status.

The status could be negative. That means no BSE is reported, and that country also has food surveillance program meeting the OIE requirements.

Then the next category would be, although no BSE is reported, but if the country does not have surveillance program, is not looking for BSE cases, then it's BSE status unknown.

Then you have BSE positive countries, have been divided into high prevalence or high risk, low prevalence, low risk.

The second factor related to the bovine source material would be the slaughtering house procedures. As Dr. Taylor mentioned earlier, for BSE countries, whether you will consider the specified risk material be removed for BSE free countries such as the United States.

The U.S. government's policy is we do not believe SRM removal as proposed by you is applicable here.

Next one. The second part of the factors will be manufacturing process and the controls. The first small category will be in the rendering process which produce edible grade and the inedible grade tallows, and we also heard that there are many different means to making edible grade tallows, the batch process, continuous process.

Then the manufacturing process for tallow derivatives: We have heard many different ways, and we know for further derivatized the derivatives, then it will go through even downstream processing.

The last factors will be the end use. For tallow it can be used in food and cosmetics, and that we do not know the status of dietary supplement. For tallow derivatives, I separate the end use into four classes: Cosmetics, topicals, and the transdermals, which are delivered through skin.

One topical put on open wound will be very similar to an injectable product. The second category will be through oral route, food, nutrition and dietary supplement and oral drugs.

Third category: Drug administered via nasal, otic, rectal and the vaginal routes. Most of them go through mucous membrane.

The fourth one, the injectable:

Ophthalmic, inhalation through bronchia or lungs, and the implantable products.

These four categories may not be proper. You may want to consider to combine them into just two, injectable and the others, or you want to divide them into more categories.

Next one. So the charge for the committee is to assess the safety of both imported and domestic tallow and the tallow derivatives, with regard to the risk posed by TSEs, specifically TSEs.

The first question: Does the available scientific information justify a change in the current FDA guidelines that bovine source material for the rendering of tallow should not come from BSE countries as designated by USDA?

If you recommend a change, then should FDA consider changes to the guidelines for tallow used in food and cosmetics? Should FDA change the criteria of sourcing countries? Should we make recommendations on the slaughtering procedure, and what are they? If the sourcing country can be from BSE countries, then should an SRM be removed? Should we make recommendations on the rendering process, and what are they? Should -- May inedible tallow be used in cosmetics?

Question 3: The next question would be on tallow derivatives. We separate them into -- We made a separation, because we think you may have different answers for the tallow from tallow derivatives. So the question will be just repeated.

Number 3: Does the available scientific information justify a change in the current FDA guidelines that bovine source material for manufacturing of tallow derivatives should not come from BSE country, as designated by USDA?

The last question: If yes, should FDA consider changes to the guidelines for tallow derivatives used in food, cosmetics, nutritional and dietary supplements, and a drug administered via various routes?

Even though we did not put down biologics and medical devices because few derivatives are used there, the recommendations to human drugs will be applicable to medical devices and the biologics.

The specific questions will be on sourcing countries and slaughtering procedures and tallow quality controls, on manufacturing process and process controls for various tallow derivatives.

Thank you.

CHAIRMAN BROWN: Thank you, Dr. Chiu.

I am, frankly, intimidated by what we're being asked to do today. This is the point when the Chairman really ought to be able to bring into focus and guide the committee's discussion and deliberation, and I don't know if I can do that.

I think the first thing to be clear about is that the third slide from the last which Dr. Chiu showed is not something that I think, frankly, this committee should be involved in, and that is a consideration of whether the entire process of producing tallow sourced in this country ought to be in some way changed or altered.

My understanding of what this committee's charge was in the written material was that we are not going to try and dictate what the rendering committee does with respect to tallow when the tallow is sourced from this country.

If we're expected to do that, we're not going to have time to do anything else this afternoon. So I would ask the committee if they agree with that. It is not, in my judgment, our business to evaluate rendering and tallow processing in this country from U.S. sources.

It wasn't a question. That's the point. It was a slide before the questions in which we were

said to be evaluating not only international but domestic procedures, and I don't want to evaluate domestic procedures, if I don't have to do it.

If that were the case, we should never have been asked to deal with gelatin, dura mater and tallow in the same meeting.

DR. HUESTON: Paul, can I -- So I'm trying to figure out. I, too, thought we were restricting our discussion on tallow and tallow derivatives --

CHAIRMAN BROWN: Through BSE countries.

DR. HUESTON: -- sourced from animals outside of the United States.

CHAIRMAN BROWN: Exactly.

DR. HUESTON: Is your concern that question number 2 leaves off all the preamble and says should FDA consider changes in guidelines for tallow used in food and cosmetics, and that could be --

CHAIRMAN BROWN: Well, I don't know. I'm looking at the sheet with the four questions that we were all handed out sometime ago, and those were the questions that Dr. Chiu read. The four questions are the questions that I would be prepared to consider.

Of course, we could punt and say no to questions 1 and 3, and immediately proceed to other subjects; but we are not going to do that.

DR. CHIU: May I make a clarification?

CHAIRMAN BROWN: Yes, please do.

DR. CHIU: If you restricted your answer to BSE-free countries, then you don't have to address the slaughter house procedure. We would very much like you to consider if you expand to BSE countries or BSE status unknown countries, then whether we should implement something on the process and on the slaughtering house procedures.

So when you said we restrict it to U.S. products, then we do not need that you make any changes. We are not expecting you to make any recommendation to the U.S. practice of rendering.

CHAIRMAN BROWN: That's fine. In other words, we're going to consider the questions as written, and we're not going to worry about the slide which preceded your question slide, which asked us to consider domestic as well as international procedures.

Maybe I'm reading more into that than everybody else is, but when I saw the word domestic, it raised a red flag. So let us then consider the questions as they were presented to us as questions. Ray?

DR. ROOS: One question related to this first question, which has to do with the guidelines

that bovine source material for the rendering of tallow should not come from BSE countries.

Maybe I need some more education about this, but kind of remembering back, I got the feeling that all of the source material for tallow has to be -- - in the United States has to be collected locally. Isn't that what we kind of spoke about at one point?

We didn't?

CHAIRMAN BROWN: No. I believe that several presenters indicated that a very small proportion of raw material tallow was imported, mostly from Canada.

DR. ROOS: From Canada?

CHAIRMAN BROWN: Yes. Well, this is --

DR. ROOS: I'm wondering whether this is a totally academic question that we're going to spend 20 minutes on which has no implication as far as practice.

CHAIRMAN BROWN: Linda.

DR. DETWILER: I think it might be academic, because USDA regulations would prohibit from BSE countries plus from high risk raw materials that would come in. I mean, they would only allow in certain processed things. So --

CHAIRMAN BROWN: Like what?

DR. DETWILER: Well, as far as tallow derivatives. Our regulations would not preclude tallow derivatives from there.

DR. ROOS: We're just talking about bovine source material for the rendering of tallow.

DR. DETWILER: Right, and our regs would prohibit that, would block them.

DR. ROOS: So should we just move on to question 3, the dura?

CHAIRMAN BROWN: No. I think the -- Let me follow that, since we're agreed that we are going to address these questions, 1, 2, 3, and 4, as the questions to be considered for the tallow stage of today's discussions.

Does the committee agree that the wording of both questions 1 and 3, from BSE countries, will be understood in our deliberations to include BSE-positive countries and BSE unknown status countries? Right. That's a clarification. Now --

DR. HUESTON: Excuse me. Can I add to your clarification?

CHAIRMAN BROWN: Yes.

DR. HUESTON: It looks to me that -- and I know people spent, no doubt, hundreds of hours framing these questions, but there's every opportunity

for confusion as to whether the first question means is the concern over the entry of bovine source materials into the United States, which is a moot point because that's already prohibited, or whether its entry into the United States or used in the United States of tallow which originated from bovine source materials. That's the --

CHAIRMAN BROWN: Yes. This is what Linda, I think, was addressing. Raw materials, source materials, the USDA prevents from coming into the U.S. for any use that relates to humans. So -- or animals.

So I guess we are talking, therefore, about the importation of tallow and/or its derivatives.

Now anybody on the committee has the right to ask anybody in the audience on specific points of information. I'm sure everybody who has presented or most people are still here. I would like one additional or -- not additional, but to be reminded of what proportion of tallow used, sold or processed in derivatives is imported. What proportion of the total U.S. production of tallow or the total U.S. use of tallow is imported? Imported. That's all we're concerned about.

MR. KILANOWSKI: Raw tallow that comes

into this country is about -- I think it was 29,000 metric tons per year coming in from --

CHAIRMAN BROWN: Right. Mostly Canada, yes.

MR. KILANOWSKI: And I would say the bulk of that is coming into and being used for fatty acids.

CHAIRMAN BROWN: Right, but that's the volume or amount of tallow being imported.

MR. KILANOWSKI: Right.

CHAIRMAN BROWN: What proportion of the total tallow use or production in this country does that represent? Was it like 100 percent?

MR. KILANOWSKI: It was like half of one percent, something like that, yes.

CHAIRMAN BROWN: Half of one percent? All right. So, basically, we're talking about a half of one percent of the tallow production or use in this country that is coming under the consideration of this committee.

DR. CHIU: May I make a clarification?

CHAIRMAN BROWN: Yes.

DR. CHIU: We also -- For example, we also import cosmetics. Cosmetics imported may contain tallow which may be sourced from BSE country or BSE free countries. So we need to also consider end

product.

CHAIRMAN BROWN: Okay. So raw tallow and anything down the line that contains tallow that is imported. I presume that's a much more important import than the tallow. Yes, Leon?

MR. FAITEK: That's one of the points I wanted to make. It's not a coincidence that we're not importing tallow. We're using very little imported tallow from BSE countries. It's prohibited. That's why those import numbers are so low.

CHAIRMAN BROWN: Well, Linda was saying that tallow per se is not prohibited. It's the raw materials that are prohibited.

DR. DETWILER: Right.

MR. FAITEK: My understanding was that tallow itself was also prohibited.

DR. DETWILER: No.

CHAIRMAN BROWN: No. That's one of the things we're considering.

DR. DETWILER: Right. Tallow -- Under USDA tallow is one of the products that is exempted, tallow and tallow derivatives, and that would be in accordance with WHO recommendations in accordance with the Office of International Epizootic recommendations.

MR. KILANOWSKI: Let me just say one more

thing. The reason that we don't have a lot of tallow coming into this country is not so much because it's prohibited. It's just that we've got an overabundance of tallow here, and it's being exported every year.

CHAIRMAN BROWN: Yes, sure.

MR. KILANOWSKI: We've got 30 percent that's being exported every year. I mean, it's kind of silly to have imports coming into this country.

CHAIRMAN BROWN: Oh, that's one of the points that was evident from your presentation, which is why I asked why we're importing anything at all.

MR. FAITEK: But is it also prohibited from importation?

CHAIRMAN BROWN: What, tallow?

MR. FAITEK: Yes.

CHAIRMAN BROWN: No. Not now. That's why we're here.

DR. ROOS: So I guess we're breaking up this question into two parts, I think, at this point. One is raw tallow, which sounds like, if you exclude Canada, we're talking about something that, I think, is kind of academic.

CHAIRMAN BROWN: Right.

DR. ROOS: And the second part of the question, which sounds so vast that I'm a bit

overwhelmed, which as I understand it has to do with every cosmetic, every food product coming in the United States that has tallow in it.

CHAIRMAN BROWN: From a BSE or --

DR. ROOS: Right. Again, I just don't know how to deal with that issue. I mean, if we decide it's a bad idea that a product has had tallow from a BSE country and is in use today for a variety of products, which sounds to me like perhaps even a reasonable statement -- you know, what's the implication of our comment that this -- I mean, is there any possibility of policing this, providing documentation?

CHAIRMAN BROWN: Well, let's get to that after we decide if it's necessary.

DR. ROOS: Well, no. Feasibility -- Unless I misunderstand --

DR. CHIU: Let me remind the committee, the current FDA policy is that if a cosmetic -- imported cosmetic, if contains tallow, that tallow must come from the bovine source of a BSE-free country. So that's already the current policy.

So the question is whether you feel tallow is -- because the process is safe enough, then we can go beyond BSE free countries.

CHAIRMAN BROWN: The comment by Kiki yesterday is relevant here. The most likely thing that the committee could do would be in the direction of relaxation. All right? Or not relaxation.

At the moment, all products that contain tallow or a tallow derivative that are sourced in either BSE+ or BSE status unknown countries are prohibited from being imported. That is the current FDA position, and we're being asked --

DR. HUESTON: So it's guidance, not --

CHAIRMAN BROWN: Well, all right, guidance. I'm not an administrator. I always lose track of guidance and regulation and law and so forth, but this is guidance. Right? We'll use the word guidance. Recommendations? Is there any better word than guidance? This is what the FDA guidance or recommendation is. Okay.

DR. HUESTON: As it relates to FDA regulated products.

CHAIRMAN BROWN: Okay. So we don't prevent the importation. We recommend the prevention of the importation.

DR. SCHONBERGER: And do we also recommend the prevention of importation of tallow from such countries?

DR. HUESTON: No. I think we need to clarify. We're talking about for use in FDA regulated products. We're not talking about banning importation. That's not the purview of the FDA. What we're talking about is the incorporation of tallow or tallow derivatives from these source materials into FDA regulated products, devices, etcetera. Did I understand that correctly?

We need to narrow our discussion a little bit. We're talking about a narrower area, I think.

DR. HELLMAN: Yes. Kiki Hellman. Will, that's exactly right, and the word is recommendation. That is what we've used all along. That may later translate into guidance, but right now it's recommendation, and Will has it exactly correct.

So the committee should decide whether there should be relaxation or a lifting of that recommendation for tallow and tallow derivatives.

DR. BURKE: Although we've gotten a listing of products that may contain tallow, I don't have any idea of what the total volume is or where these are coming from. We've talked about sources for the source material. We've talked about sources of the tallow itself, but we have not talked about the sources of who makes the cosmetics and who -- where

are the interests that say that, if this is lifted, what are the implications of this? I have no idea of what the kinetics here in terms of dollars or grams or people or anything else.

CHAIRMAN BROWN: Does anybody in the audience or the spectators have advice on this? Yes?

DR. GREEN: Well, the question, as far as the derivatives --

DR. BURKE: It's not the derivatives I'm asking right now. I'm asking just for tallow itself that goes into products.

DR. GREEN: All right.

DR. BURKE: We're going to address the derivatives, which is a separate one.

CHAIRMAN BROWN: Well, we've been told that tallow per se imported represents essentially a trivial --

DR. BURKE: But that's tallow. That's not processed tallow that is in a cosmetic already.

CHAIRMAN BROWN: That's right. So your question is what is the implication of a recommendation that products in which tallow would be used coming from BSE+ countries.

DR. BURKE: How much manufacturing is made in France? I don't have any idea.

CHAIRMAN BROWN: Yes. Right. Or more appropriately, the UK. Anybody in the FDA have a notion about that?

DR. HONSTEAD: I think the committee needs to orient its decisions based towards the scientific aspects of this thing. Part of FDA's job is to then take your scientific opinion and information and evaluation and merge that with the economics and the enforcement side of it.

So I would limit your debates here to the scientific issues.

CHAIRMAN BROWN: I think that's an excellent point, and it's a point that sometimes we on the committee forget. That's a key word in the question and always has been -- scientific. Barbara?

MS. HARRELL: Are we generally going on -- or is there anything else we're going on besides Dr. David Taylor's study as far as the scientific evidence or information? Is that all we have to go on?

CHAIRMAN BROWN: With respect to tallow, I think that is correct. I'm unaware of --

DR. HUESTON: Epidemiologic.

CHAIRMAN BROWN: I beg your pardon?

DR. HUESTON: And the epidemiologic.

CHAIRMAN BROWN: Yes, sure. There was the

phenomenon of a lack of association between the occurrence of BSE and --

MS. HARRELL: You mean the risk assessment? Which one?

DR. LURIE: I understood it -- Perhaps this was discussed, you know, in a previous version of this committee, but there's an ecological study which looks at the use of where tallow is fed to animals and the relationship between that.

CHAIRMAN BROWN: That's right.

DR. LURIE: And I have to say for myself that, without having seen the study, the design of it, there's little to convince me of the safety of tallow. It seems to me that simply by its ecological design, it adds, you know, very little to what we know. But in any case, that's not -- That's different than the risk assessment.

CHAIRMAN BROWN: The evidence, such as it is, as you say, ecological or epidemiological, was simply a failure of association of the occurrence of BSE and the distribution of tallow. That was one little clue.

DR. LURIE: Yes.

CHAIRMAN BROWN: The other little clue is Dr. Taylor's double study on tallow, both with respect

to BSE and, David, with respect to scrapie as a spike? Yes. In both of those studies which David provided a certain number of qualifications for in terms of conclusions, that is the total laboratory evidence on the absence of infectivity in tallow.

Did you have a comment?

MR. LAMBERT: Yes. Lark Lambert, Office of Cosmetics and Colors. In response to Dr. Burke's question, in our voluntary registration program these are the products that were -- that contain tallow, and you can see there's a very few on the righthand side. The number -- The 01C, that's a product category which is also other baby products, which in this case was shampoo. There was only two products.

These are out of -- Again, the companies voluntarily send in their products to be registered with the FDA. Most of them don't send it in, but if -- There are approximately 16,000 registered products.

For just tallow, not tallow derivatives, these are the product categories that they are under. You can see, most of them fall under bath soaps and detergents and, you know, shampoos are only two. So there's only a small number, really.

DR. BURKE: Thank you. That is helpful, and I do apologize for overextending into the economic

sphere, but I think it is useful to have information on products, routes, dosage and grams. I think those are all part of legitimate scientific components of any decision, and that is useful. Thank you.

CHAIRMAN BROWN: And I think the committee is -- Yes?

DR. OLANDER: One last question. What is the procedure or methods for verifying that we are receiving products that are derived from edible tallow as opposed to inedible tallow from overseas countries?

CHAIRMAN BROWN: Anybody wish to answer that question? Any of the speakers?

DR. HUESTON: Don't they have to have USDA inspection to show that at least meet the USDA? I was looking at Bob.

CHAIRMAN BROWN: Microphone, please.

DR. BREWER: They would have to have an export certificate accompanying this signed by an official in the country that it was being exported from, the United States. Then that certificate would be examined when it came into the United States, of course, by the USDA authority, either an APHIS or an FSIS authority, and you would have to be satisfied that what they have stated on the certificate was accurate and that the product was accurately

described.

DR. HUESTON: Wouldn't edible tallow, since it's coming from essentially animals that are passed -- They would have to meet the same requirements and have to have a USDA inspector there to have equivalency.

DR. BREWER: They would have to have a ante mortem and post mortem inspection, be handled in a separate facility from the inedible. In other words, you couldn't process edible tallow in the morning and inedible in the afternoon and that type of thing. Have to be a facility dedicated just to producing edible product.

Now as far as I know, nothing comes except from Canada in the way of an edible tallow product, and I suspect that's mostly from a couple of plants that are owned by U.S. interests. So that's probably the reason for that.

DR. HUESTON: Are you aware of anything from Europe, Linda?

MR. ANDERSON: One other comment. Even on the slide that was put up there about the products that they register as having tallow as part of the ingredient, if you go back, I'm sure you're going to find that a lot of those are really derivatives, not

raw tallow that are going into those products.

So, I mean, there's a very, very small amount of edible tallow or tallow used in those products in its native form. It would be in a derivative or further processed form.

CHAIRMAN BROWN: Again, to come back to the question 1, as it's worded, we're excused, I think, from concentrating on raw materials, because that's the way the question is worded. Guidelines that bovine source materials for the rendering of tallow should not come from BSE countries.

Answering that question takes care of everything downstream. Now if we decide that there should be some relaxation of this, then we have to get into the downstream side of things, and that's why the slides that you have seen presented by the FDA have broken the use down into things like injectables and orals and cosmetics.

If we get into saying yes to question 1 -- that is, scientific information does justify a change -- then we are going to get into areas downstream, which is overall use products and so forth.

As I say, one of the things you have to sort of ask yourself is if -- you have to assume that this is designed to prevent an infectious unit of BSE

from entering the U.S. as tallow or tallow derivative, and you have to assume that this is designed with that in mind.

Let us suppose that a cow from a herd in the United Kingdom is slaughtered and the tallow is pooled with other cattle tallow, and that's imported for a use or another, an injectable, an oral, a cosmetic. Is that something that you feel would be -- would carry such a low risk that it would not be a problem and, therefore, we would change the FDA restrictions; or do you feel that that does pose "an unacceptable risk" or an unnecessary risk, in which case we leave the FDA current policy intact?

DR. ROOS: Well, I mean, the data that we have, as I see it, demonstrates no infectivity of tallow, although the data is a little bit limited. It seems like there is a very small amount of protein present in this tallow, which also makes one a little bit confident that one doesn't have the infectious agent.

Generally, one is dealing here with a species/species barrier, if one is talking about these tallow products, and I'm just talking about raw tallow for human use; and lastly, we have some processing which involves heat and alkali treatment.

I guess I would ask you, Paul or anyone else, how you felt about the processing of this raw tallow with respect to the heat and the treatment used and how much confidence we should have with respect to that.

If there are issues still remaining with respect to the infectivity and the heat and the alkali treatment, and one is dealing with a BSE country in which BSE is clearly present, I wonder whether one should at this point in time maintain regulations with respect at least to these tallow products, which sound like they're a very small amount of material coming in, at any rate, although I would raise questions as to how many products one is really dealing with and whether, in fact, all these -- crude tallow might also be tallow derivatives.

It's going to get very complicated restricting one and not the other. At any rate, I just wanted to know whether you could put the heat and the alkali treatment in perspective here. No alkali treatment, just heat treatment.

If you remember back to these crude --

CHAIRMAN BROWN: Yes. Well, the tallow --

DR. SCHONBERGER: Can I expand on that, the question, and maybe focus for a moment on Fred

Bader's model. He used 10^{-6} for arbitrary reduction for the tallow derivative. The question would be what would be the comparable figure that you would use for tallow for the effect of the production on the reduction of titer? Would you use something more like 10^{-3}? Is that a better estimate if we were to just consider tallow, given what Ray is asking?

CHAIRMAN BROWN: David produced evidence that the rendering process per se used in most of Europe, with the exception of the autoclave type rendering process -- and tallow is a product of the rendering process -- that all of the other procedures had negligible infectivity reduction.

Says nothing about the infectivity at the start. All we're talking now is about a process. The process of rendering is not an effective inactivant of these agents, and one of the products of the rendering process is tallow, which leads me to just summarize the improbabilities of infectivity.

Number one, a BSE cow that is clinically healthy is a possibility of occurring, but it's unusual. All right? I mean, at the present moment, even in the UK presumably, you have cattle that will come down with BSE that are presently healthy. So the UK is a little special. The other countries are much

less at risk than that.

So the probability of including an cow incubating BSE in the rendering process is a small one. It exists in a BSE country, but that's the first improbability.

The second improbability is --

DR. SCHONBERGER: Well, again, for putting numbers on it, I think in Bader's model it was like it changed to 1 to 10,000 or something.

CHAIRMAN BROWN: I think you would be making a mistake to play those mathematical games at this point. I just don't think there's enough solid evidence to make that a worthwhile route to follow.

DR. SCHONBERGER: I was just trying to go through this exercise in part with Bader's model to see if I was still going to be in the insignificant risk category. If you're telling me that that 10^{-8} has to be thrown out because -- totally -- then he ended up with a 10^{-15}, which was a negligible risk.

If I'm going to add an eightfold increase to that, I'm already starting to get into the significant risk.

CHAIRMAN BROWN: I wouldn't argue from Dr. Bader's conclusion. I think the conclusions he drew were valid conclusions with the assumptions that he

used, but he -- I mean, to get all those assumptions, Dr. Bader would have to come back up here and give us a 15 minute lecture on the assumptions for that particular number.

All I'm saying is that, number one, the improbability of having a BSE infected cow in the rendering process. It would occur, and that's why the BSE countries are called BSE countries, but that's one improbability.

The second improbability is the infectivity, the presence of infectivity in the tissues that are being rendered.

The third improbability is the survival of those infected units after processing. There's a little bit, according to David's analysis -- there's a slight reduction from that process, but short of the process of pressure/heat combination, the reduction is really quite small.

So those are the improbabilities, and those are what we would have to consider and weigh if we say that the FDA can relax a little bit. We have to understand that this is the kind of evaluation we're going to have to get into if we say the FDA can relax on tallow or raw product sources of tallow and tallow products, not tallow derivatives. That's not

this question. This is tallow.

DR. SCHONBERGER: Well, it sounds as if we're dealing with an extremely low risk, but one that may be above what Bader had described as the insignificant level at 10^{10} or something in that area. That's where I'm sort of leaning, and I'm just throwing that out for others to maybe comment and say that we haven't heard anything today to put us into the absolutely insignificant risk category for tallow, and that, therefore, we should change the policy.

That's where I'm leaning right now.

CHAIRMAN BROWN: Well, I certainly agree that the scientific evidence bearing on the question is very limited. Such as it is, it inspires confidence, but it's very limited. Is that fair, David? Wake up.

DR. TAYLOR: Are you asking for comments?

CHAIRMAN BROWN: Yes. The evidence with respect to lack of infectivity in tallow is very, very limited in scope. Such as it is, it inspires confidence.

DR. TAYLOR: Yes, I would agree with that. I would also say that the figures that I've played around with early on which we discussed somewhat, although you can argue with the detail of them, they

do give some idea of the scale of safety that could be associated with tallow.

CHAIRMAN BROWN: It's, in a sense, ironic that the FDA has got us considering, of all the kinds of things that I could imagine coming from BSE infected cattle, a couple of items that are so low down the list of dangerous sources. I mean, it's not like we're dealing with the importation of thymus for baby food. It's really quite a different question.

I don't think we should lose sight of that.

DR. SCHONBERGER: Well, going back to what Bader was asking us to consider was the other side of the equation, is what do we gain by a decision to change? You know, what's the problem that we create by not changing the recommendation and, given what we heard --

CHAIRMAN BROWN: What problem do we create?

DR. SCHONBERGER: You know, when we talked about blood safety and we talk about withdrawing, we had the problem of are we creating a shortage?

CHAIRMAN BROWN: That's the FDA's problem. That is specifically not our problem.

DR. SCHONBERGER: I know.

CHAIRMAN BROWN: Nor should we be considering it.

DR. SCHONBERGER: Well, I thought Bader was trying to tell us to evaluate the -- that there is no zero risk and that this is a risk/benefit type of decision.

CHAIRMAN BROWN: Right. But the FDA was telling us forget the benefits.

DR. SCHONBERGER: I don't -- They were telling us --

CHAIRMAN BROWN: They're going to decide about the benefits. It's their decision to decide risk/benefit analyses. It's our decision to make an estimate of risk.

DR. SCHONBERGER: All right. Well, then I'll just state it so that --

CHAIRMAN BROWN: Is that fair? Is that correct? I mean, would you say that that's what we should be doing? I mean, it's your job to decide about risk/benefit.

DR. HONSTEAD: That's true, Dr. Brown, and it's specific in the question, and it has scientific in it.

DR. CHIU: I think the committee shouldn't -- the benefits to human health, not the benefit

economically, because that's our problem.

DR. SCHONBERGER: Okay. Well, I'll talk in terms of human health then. So the committee -- or the FDA can take that into consideration when they're on their own. I really think we're probably dealing with a non-problem or a problem that's very low, approaching that insignificant level; but I can't be sure from what I heard today that it really is in the insignificant category.

Then I look at the other side and say what's the impetus for me to change these recommendations. What is the problem that exists, if I don't say change it, and I don't see a problem there. So I say why should we do it? That's sort of where I'm at, and I'm opening that up, if people want to go after that.

DR. LURIE: I think that the notion of restricting ourselves to the scientific is on its face attractive, but in practice not really reasonable. I think Don sort of hinted at this.

Part of the scientific question has to do with the degree of exposure of people to the likely or not very likely infectious materials, and that is, in and of itself, related to, you know, the amount of imported material and so forth and so on.

I see it the way you're seeing it, which is that, in effect, the risk of continuing the current FDA policy has not been identified by any speaker that I've heard at this meeting. I have not heard anybody say that there are particularly important products that will somehow not come here. I have not heard that there are any particular medication that will somehow be denied to American consumers as a result of continuing the ban. I have not heard that the existing ban has created that kind of problem.

All of the evidence seems to suggest that the required tallow is available in abundance and that the existing policy has caused no problem. Agreeably, the risks may be small, but it doesn't seem things are broke. So I'm not sure why we need to fix it.

CHAIRMAN BROWN: Comments? Do you want to vote? We're talking again about question number one, tallow as opposed to tallow derivatives. This is just with respect to tallow, and the question is -- and I come back to the word scientific.

I really do think we can limit it to scientific, and I don't think it necessarily boils down to the question of what risks are we taking by not changing it. I think we have maybe more responsibility than that.

I think we have to look at what we heard today and decide whether or not BSE sourced tallow -- excuse me, BSE sourced tallow -- BSE country sourced tallow poses any significant risk to this country and decide whether or not, if it does, then we leave the FDA regulations as they are, intact. If we think that that risk for whatever product -- and we can identify products. We can say, well, cosmetics don't seem to me to be a particular risk, but injectables are.

We have the ability to say to the FDA, yes, continue your restrictions on anything that has this source for injectables or for cosmetics, but relax a little bit on something else.

So it's not a blanket thing. It's not all or nothing. We can decide to recommend to the FDA that they relax on certain things. It's not an umbrella. It's not 100 percent. We have the ability to specify materials which we feel really don't pose a risk and, if so, then there's no logical reason to continue acting as though they do. Paul?

DR. HUESTON: Paul, can I ask just -- I appreciate very much the framework you're setting. Can I try to take that one step further.

If one looks at it at least from my perspective, trying to categorize or evaluate the

risks, certainly, one would say that inedible tallow from inedible rendering has more high risk input material than material going into edible rendering. Follow me?

CHAIRMAN BROWN: Yes.

DR. HUESTON: Because edible rendering is using materials that would be passed for human consumption. So we get back to the analogy that, in fact, you could eat -- you can buy in the store and eat everything that goes into edible rendering. Correct?

CHAIRMAN BROWN: Yes. Absolutely.

DR. HUESTON: Now for -- Part number two then, if we talk about BSE countries, and I think the real countries we're talking about here are really European countries -- So most of those is -- just another side question. Do brain and spinal cord -- do the SRMs currently enter the pool of raw materials for developing edible rendering?

DR. TAYLOR: Not in the UK and not in some other countries, but not in all European member states.

DR. HUESTON: Okay, because in some European member states one can actually still consume brain and spinal cord, if you so desire.

DR. TAYLOR: Exactly.

DR. HUESTON: We know that the processing -- So I think we have a differentiation here between -- In the United States, in fact, we also can eat brain and spinal cord, if we so desire. Right? So we have a differentiation between those things -- the tallow from edible rendering which would normally come into our diet anyway and the tallow from inedible rendering, which includes a whole lot of other things.

It includes most of the high risk animals and a larger proportion of the high risk materials. I'm just trying to help give a framework to it, because I think that comes back then to the uses and to this very nice chart that we have of clarifying where might the tallow enter our -- enter the opportunity to expose.

So as Dr. Lurie is saying, where might be the exposure, and what would be the type of products or the origin of the tallow used in those types of products for which United States citizens might get exposure?

CHAIRMAN BROWN: Why don't we vote on a first approximation, which is do you think that the current FDA blanket restrictions or recommendations to avoid BSE or BSE unknown status countries should

continue to apply; or can we make here today at least some revisions which will open that umbrella and put a few holes in it. Leon?

MR. FAITEK: You clarified it.

CHAIRMAN BROWN: Okay. I'd like to vote on that, and then if we decide that there are certain things which should be relaxed, then that's the next topic of discussion, to decide what those things are.

MR. FAITEK: You're asking us to vote on--

CHAIRMAN BROWN: On question 1.

MR. FAITEK: -- question 1 plus or --

CHAIRMAN BROWN: Just question 1, period. Okay?

DR. FREAS: Dr. Brown, could I just clarify for the audience and for the record that there are currently 11 voting members at the table. Our industry representative and the two guests that have been invited to the table are nonvoting at this time.

CHAIRMAN BROWN: And the members of the committee may choose to not vote, vote with a short statement, vote with a Larry Schonberger type statement, vote yes, vote no, or abstain. Don?

DR. FRANCO: Abstain.

CHAIRMAN BROWN: Larry?

DR. SCHONBERGER: I'll abstain.